

CLAIMS

We claim:

1 **[0168] 1.(currently amended)** A method comprising the steps of:
2 positioning a probe adjacent a tissue site of an animal including a human;
3 acquiring pre-injection data of the tissue site;
4 injecting a contrast agent into the animal at an injection site;
5 acquiring ~~acquiring data before and after injection~~ post-injection data of the tissue site;
6 performing a difference analysis between pre-injection data and post-injection data to detect,
7 localize, and quantify anatomical, morphological and/or functional features of the tissue site.

[0169] 2.(canceled)

[0170] 3.(canceled)

[0171] 4.(canceled)

[0172] 5.(canceled)

[0173] 6.(canceled)

[0174] 7.(canceled)

[0175] 8.(canceled)

[0176] 9.(canceled)

[0177] 10.(canceled)

[0178] 11.(canceled)

[0179] 12.(canceled)

[0180] 13.(canceled)

[0181] 14.(canceled)

[0182] 15.(canceled)

[0183] 16.(canceled)

[0184] 17.(canceled)

[0185] 18.(canceled)

[0186] 19.(canceled)

[0187] 20.(canceled)

[0188] 21.(canceled)

[0189] 22.(canceled)

[0190] 23.(canceled)

[0191] 24.(canceled)

[0192] 25.(canceled)

[0193] 26.(canceled)

[0194] 27.(canceled)

[0195] 28.(canceled)

[0196] 29.(canceled)

[0197] 30.(canceled)

[0198] 31.(canceled)

[0199] 32.(canceled)

[0200] 33.(canceled)

[0201] 34.(canceled)

[0202] 35.(canceled)

[0203] 36.(canceled)

[0204] 37.(canceled)

[0205] 38.(canceled)

[0206] 39.(canceled)

[0207] 40.(canceled)

[0208] 41.(canceled)

1 [0209] 42.(new) The method of claim 1, further comprising the steps of:
2 prior to the injecting step, positioning a contrast agent delivery system adjacent the injection
3 site.

1 [0210] 43.(new) The method of claim 1, wherein the pre-injection data comprises a pre-
2 injection data sequence of the tissue site acquired over a pre-injection period of time.

1 [0211] 44.(new) The method of claim 1, wherein the post-injection data comprises a post-
2 injection data sequence of the tissue site acquired over a post-injection period of time.

1 **[0212] 45.(new)** The method of claim 1, wherein the difference analysis is between the pre-
2 injection data sequence and post-injection data sequence.

1 **[0213] 46.(new)** The method of claim 1, wherein the injection site comprises a vessel.

1 **[0214] 47.(new)** The method of claim 46, wherein the vessel comprises an artery supply blood
2 to the tissue site or a vein removing blood from the tissue site.

1 **[0215] 48.(new)** The method of claim 46, wherein the tissue site is a vessel and the step of
2 positioning the probe comprises the steps of:
3 positioning a guide-catheter in the vessel; and
4 positioning, on the guide-catheter, a micro-catheter including the probe in the vessel adjacent
5 the tissue site.

1 **[0216] 49.(new)** The method of claim 1, further including the step of:
2 acquiring during injection data sequence,
3 wherein the performing step further includes difference analyses of the pre-injection, during-
4 injection and post-injection data sequences.

1 **[0217] 50.(new)** The method of claim 1, wherein the data comprises ultrasonic data.

1 **[0218] 51.(new)** The method of claim 49, wherein the data comprises ultrasonic data.

1 **[0219] 52.(new)** The method of claim 1, wherein the pre-injection data comprises a pre-
2 injection data sequence of the tissue site acquired over a pre-injection period of time and the post-
3 injection data comprises a post-injection data sequence of the tissue site acquired over a post-
4 injection period of time.

1 **[0220] 53.(new)** The method of claim 52, further comprising the step of:
2 forming pre phase-correlated data from the pre-injection data and post phase-correlated data

from the post-injection data.

[0221] 54.(new) The method of claim 53, further comprising the step of:
selecting a region of interest within the pre and post phase-correlated data.

[0222] 55.(new) The method of claim 54, further comprising the step of:
compensating for relative motion of the region of interest in the pre and post phase-correlated
data.

[0223] 56.(new) The method of claim 55, further comprising the step of:
filtering the motion compensating pre and post phase-correlated data.

[0224] 57.(new) The method of claim 56, further comprising the step of:
reconstruction the filtered, motion compensated pre and post phase-correlated data.

[0225] 58.(new) The method of claim 57, further comprising the step of:
identifying enhancements in the region of interest as a function of a data acquisition time.

[0226] 59.(new) The method of claim 52, wherein the data acquisition times are from about
0.5 minutes to about 30 minutes.

[0227] 60.(new) The method of claim 52, wherein the pre-injection data is acquired over a pre-
injection period of time ranging from about 1 second to about 10 minutes and the post-injection data
is acquired over a post-injection period of time ranging from about 1 second to about 20 minutes.

[0228] 61.(new) The method of claim 1, wherein the data is digitized and automatically sorted
and binned according to their temporal position in each of a sequence of cardiac phases over the total
acquisition time.

[0229] 62.(new) The method of claim 1, further comprising the step of:
generating difference data or image sequences between data or frames in the pre- and post-

3 injection data.

1 [0230] 63.(new) The method of claim 1, further comprising the step of:
2 performing noise reduction on the data prior to difference analysis via mathematical
3 averaging of temporally correlated data or frames, where temporal correlated data or images are data
4 or images binned at a same point in a cardiac cycle.

1 [0231] 64.(new) The method of claim 1, further comprising the step of:
2 automatically thresholding the difference data or images to separate regions of salient grey-
3 level enhancements.

1 [0232] 65.(new) The method of claims 64, further comprising the step of:
2 color-coding the thresholded difference data or images to indicate a location and strength of
3 the enhancements.

1 [0233] 66.(new) The method of claim 1, further comprising the step of:
2 generating an animation of changes in enhancements over the total acquisition time of the
3 difference data or images, thresholded data or images and/or the color-coded data or images.

1 [0234] 67.(new) The method of claim 66, wherein the animation corresponds temporally with
2 the originally-acquired data in order to allow direct visual comparison between the original data and
3 the processed data.

1 [0235] 68.(new) The method of claim 1, further comprising:
2 computing a statistical measurement of an average enhancement per enhanced pixel for each
3 difference data or image generated over the total acquisition time to quantify numerically a presence
4 and amount of enhancements over time.

1 [0236] 69.(new) The method of claims 68, wherein the enhancements are evidence of vasa
2 vasorum or other structures associated with the site.

1 [0237] 70.(new) The method of claim 69, wherein the other structures include plaque, calcified
2 plaque, malignancy structure, malignancy vascularization.

1 [0238] 71.(new) The method of claim 1, wherein the probe is selected from the group
2 consisting of an ultrasound probe, a variable frequency ultrasound probe, a magnetic probe, a
3 photonic probe, a near Infrared probe, a terrahertz probe, microwave probe and combinations thereof.

1 [0239] 72.(new) The method of claim 1, wherein the contrast agent is selected from the group
2 consisting of microbubbles, magnetically active microbubbles, magnetically active nanoparticles,
3 near Infrared visible microbubbles, near Infrared visible nanoparticles, optically visible
4 microbubbles, optically visible nanoparticles, terrahertz visible microbubbles, terrahertz visible
5 nanoparticles, microwave visible microbubbles, microwave visible nanoparticles, red blood, cells
6 including magnetically active nanoparticles, near Infrared visible nanoparticles, optically visible
7 nanoparticles, terrahertz visible nanoparticles, microwave visible nanoparticles, and mixtures
8 thereof, and mixtures or combinations thereof.

1 [0240] 73.(new) The method of claim 1, further comprising the step of:
2 exposing the tissue site, after contrast agent injection, to a sonic energy at a frequency
3 sufficient to cause a position of each contrast agent to periodically change.

1 [0241] 74.(new) The method of claim 1, further comprising the step of:
2 exposing the site, after contrast agent injection, to a sonic energy at a frequency sufficient
3 to destroy the contrast agent.

1 [0242] 75.(new) A method comprising the steps of:
2 positioning a probe adjacent a tissue site of an animal including a human,
3 acquiring pre-altered blood flow data of the tissue site,
4 positioning a balloon in an artery supplying blood to or a vein removing blood from the tissue
5 site,
6 altering a blood flow to the tissue site by inflating or partially inflating the balloon,
7 acquiring during-altered blood flow data of the tissue site,

8 deflating the balloon,
9 acquiring post-altered blood flow data of the tissue site,
10 performing a difference analysis between pre-altered blood flow data, during-altered blood
11 flow data and post-altered blood flow data to detect, localize, and quantify anatomical,
12 morphological and/or functional features of the tissue site..

1 **[0243] 76.(new)** The method of claim 75, wherein the inflating and deflating steps are
2 performed periodically at a given periodicity.

1 **[0244] 77.(new)** The method of claim 75, wherein red blood cells act as a contrast agent.

1 **[0245] 78.(new)** A catheter apparatus comprising:
2 a guide-catheter adapted to be inserted into a peripheral vessel of an animal including a
3 human and positioned in a target vessel; and
4 a contrast agent delivery system designed to inject an amount of contrast agent into the
5 vessel.

1 **[0246] 79.(new)** The apparatus of claim 78, further comprising:
2 at least one guide-wire adapted to be extended from a distal end of the guide-catheter into
3 the vessel; and
4 at least one micro-catheter having an central orifice and adapted to slide down the guide wire
5 to a desired location in the vessel.

6 **[0247] 80.(new)** The apparatus of claim 79, further comprising:
7 a balloon adapted to augment a flow of blood in the vessel.

1 **[0248] 81.(new)** The apparatus of claim 79, wherein the micro-catheter includes a probe.

1 **[0249] 82.(new)** The apparatus of claim 79, wherein the micro-catheter includes a plurality of
2 probes.

1 [0250] 83.(new) The apparatus of claim 79, wherein the contrast agent delivery system forms
2 a part of the micro-catheter.

1 [0251] 84.(new) The apparatus of claim 79, wherein the contrast agent delivery system is
2 upstream of the probe or probes.

1 [0252] 85.(new) The apparatus of claim 80, wherein the balloon is upstream of the probe .

1 [0253] 86.(new) The apparatus of claim 81, wherein the probe is selected from the group
2 consisting of an ultrasound probe, a variable frequency ultrasound probe, a magnetic probe, a
3 photonic probe, a near Infrared probe, a terrahertz probe, microwave probe and combinations thereof.

1 [0254] 87.(new) The apparatus of claim 78, wherein the contrast agent is selected from the
2 group consisting of microbubbles, magnetically active microbubbles, magnetically active
3 nanoparticles, near Infrared visible microbubbles, near Infrared visible nanoparticles, optically
4 visible microbubbles, optically visible nanoparticles, terrahertz visible microbubbles, terrahertz
5 visible nanoparticles, microwave visible microbubbles, microwave visible nanoparticles, red blood,
6 cells including magnetically active nanoparticles, near Infrared visible nanoparticles, optically visible
7 nanoparticles, terrahertz visible nanoparticles, microwave visible nanoparticles, and mixtures
8 thereof, and mixtures or combinations thereof.